WHAT IS CLAIMED IS:

1. A compound of the formula I or formula II:

5 I

10 wherein:

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X is selected from O, N, S, SO₂ and C;

Y is selected from -O-, -NR¹²-, -S-, -SO-, -SO₂-, and -CR¹²R¹²-, -NSO₂R¹⁴-, -NCOR¹³-, -CR¹²COR¹¹-, -CR¹²OCOR¹³-, -CO-;

Z is independently selected from C or N, where at least one Z is N and at most two Z are N;

R¹ is selected from: -C₁-6alkyl, -C₀-6alkyl-O-C₁-6alkyl, -C₀-6alkyl-S-C₁-6alkyl, -(C₀-6alkyl)
(C₃-7cycloalkyl)-(C₀-6alkyl), hydroxy, heterocycle, -CN, -NR¹²R¹², -NR¹²COR¹³,
NR¹²SO₂R¹⁴, -COR¹¹, -CONR¹²R¹², phenyl, and pyridyl,

where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C₁₋₃alkyl, trifluoromethyl, C₁₋₃alkyl, -O-C₁₋₃alkyl, -COR¹¹, -SO₂R¹⁴, -NHCOCH₃, -NHSO₂CH₃, -heterocycle, =O, -CN.

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where the phenyl and pyridyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, COR¹¹, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl;

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where R¹¹ is independently selected from: hydroxy, hydrogen, C₁₋₆ alkyl, -O-C₁₋₆alkyl, benzyl, phenyl and C₃₋₆ cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆ alkyl, and trifluoromethyl,

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where R¹² is selected from: hydrogen, C₁₋₆ alkyl, benzyl, phenyl and C₃₋₆ cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl, and trifluoromethyl,

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where R¹³ is selected from: hydrogen, C₁₋₆ alkyl, -O-C₁₋₆alkyl, benzyl, phenyl and C₃₋₆ cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl, and trifluoromethyl, and

where R¹⁴ is selected from: hydroxy, C₁₋₆ alkyl, -O-C₁₋₆alkyl, benzyl, phenyl and C₃₋₆ cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆ alkyl, and trifluoromethyl;

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 R^2 is selected from: hydrogen, C_{1-3} alkyl, unsubstituted or substituted with 1-3 fluoro, -O- C_{1-6} alkyl, unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl, heterocycle, and nothing, and O, when the Z bonded to R^2 is N;

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R³ is selected from: hydrogen, C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, -O-C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl, heterocycle, and nothing, and O, when the Z bonded to R² is N;

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R⁴ is selected from: hydrogen, C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, -O-C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl, heterocycle, and nothing, and O, when the Z bonded to R² is N;

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R⁵ is selected from: C₁₋₆alkyl, unsubstituted or substituted with 1-6 substituents selected from fluoro and hydroxyl, -O-C₁₋₆alkyl, unsubstituted or substituted with 1-6 fluoro, -CO-C₁₋₆alkyl, unsubstituted or substituted with 1-6 fluoro, -S-C₁₋₆alkyl, unsubstituted or substituted with 1-6 fluoro, -pyridyl, unsubstituted or substituted with one or more substitutents selected from: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹, fluoro, chloro, bromo, -C₄₋₆cycloalkyl, -O-C₄₋₆cycloalkyl, phenyl, unsubstituted or substituted with one or more substituents selected from:

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halo, trifluoromethyl, C_{1-4} alkyl, and COR^{11} , -O-phenyl, unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C_{1-4} alkyl, and COR^{11} , - C_{3-6} cycloalkyl, unsubstituted or substituted with 1-6 fluoro, -O- C_{3-6} cycloalkyl, unsubstituted or substituted with 1-6 fluoro, -heterocycle, -CN, and - COR^{11} ;

R⁶ is selected from: hydrogen, C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, -O-C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl, heterocycle, and nothing, and O, when the Z bonded to R² is N;

R⁷ is selected from: hydrogen, (C₀-6alkyl)-phenyl, (C₀-6alkyl)-heterocycle, (C₀-6alkyl)-C₃-7cycloalkyl, (C₀-6alkyl)-COR¹¹, (C₀-6alkyl)-(alkene)-COR¹¹, (C₀-6alkyl)-SO₃H, (C₀-6alkyl)-W-C₀-4alkyl, (C₀-6alkyl)-CONR¹²-phenyl, (C₀-6alkyl)-CONR²⁰-V-COR¹¹, and nothing, when X is O, S, or SO₂,

where W is selected from: a single bond, -O-, -S-, -SO-, -SO₂-, -CO-, -CO₂-, -CO-, -CO₂-, -CO-, -CO₂-, -CO-, -CO₂-, -CO-, -SO₂-, -CO-, -SO₂-, -CO-, -CO₂-, -CO-, -SO₂-, -CO-, -SO₂-, -CO-, -CO₂-, -CO-, -SO₂-, -CO-, -SO₂-, -CO-, -SO₂-, -CO-, -CO₂-, -CO-, -SO₂-, -SO₂-, -CO-, -SO₂-, -CO-, -SO₂-, -CO-, -SO₂-, -SO₂

where V is selected from C₁₋₆alkyl or phenyl,

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where R²⁰ is hydrogen or C₁₋₄alkyl, or where R²⁰ is joined via a 1-5 carbon tether to one of the carbons of V to form a ring,

where the C₀₋₆alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, hydroxy, -C₀₋₆alkyl, -O-C₁₋₃alkyl, trifluoromethyl, and -C₀₋₂alkyl-phenyl,

where the phenyl, heterocycle, cycloalkyl, and C0-4alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C1-3alkyl, -O-C1-3alkyl, -C0-3-COR 11 , -CN, -NR 12 R 12 , -CONR 12 R 12 , and -C0-3-heterocycle,

or where the phenyl and heterocycle may be fused to another heterocycle, which itself may be unsubstituted or substituted with 1-2 substituents independently selected from hydroxy, halo, -COR¹¹, and -C₁₋₃alkyl, and

where alkene is unsubstituted or substituted with 1-3 substituents which are independently selected from: halo, trifluoromethyl, C_{1-3} alkyl, phenyl, and heterocycle;

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 R^8 is selected from: hydrogen, nothing when X is either O, S, SO_2 or N or when a double bond joins the carbons to which R^7 and R^{10} are attached, hydroxy, C_{1-6} alkyl, C_{1-6} alkyl-hydroxy, -O- C_{1-3} alkyl, - COR^{11} , - $CONR^{12}R^{12}$, and -CN;

where R⁷ and R⁸ may be joined together to form a ring selected from: 1H-indene, 2,3-dihydro-1H-indene, 2,3-dihydro-benzofuran, 1,3-dihydro-isobenzofuran, 2,3-dihydro-benzothiofuran, 1,3-dihydro-isobenzothiofuran, 6H-cyclopenta[d]isoxazol-3-ol, cyclopentane, and cyclohexane,

where the ring formed is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C_{1-3} alkyl, - C_{0-3} COR¹¹, -CN, - $NR^{12}R^{12}$, - $CONR^{12}R^{12}$, and - C_{0-3} -heterocycle, or

where R^7 and R^9 or R^8 and R^{10} may be joined together to form a ring which is phenyl or heterocycle,

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wherein the ring is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from: halo, trifluoromethyl, hydroxy, C₁₋₃alkyl, -COR¹¹, -CN, -NR¹²R¹², and -CONR¹²R¹²;

R⁹ and R¹⁰ are independently selected from: hydrogen, hydroxy, C₁₋₆alkyl, C₁₋₆alkyl-COR¹¹, C₁₋₆alkyl-hydroxy, -O-C₁₋₃alkyl, =O, when R⁹ or R¹⁰ is connected to the ring via a double bond, and halo;

 R^{15} is selected from: hydrogen, and C_{1-6} alkyl, unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -CO₂H, -CO₂C₁₋₆alkyl, and -O-C₁₋₃alkyl;

- R¹⁶ is selected from: hydrogen, C₁₋₆alkyl, unsubstituted or substituted with 1-6 substituents

 selected from: fluoro, C₁₋₃alkoxy, hydroxyl and -COR¹¹, fluoro, -O-C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, C₃₋₆ cycloalkyl, -O-C₃₋₆cycloalkyl, hydroxy, -COR11, and -OCOR¹³, or R¹⁵ and R¹⁶ are joined together via a C₂₋₄alkyl or a C₀₋₂alkyl-O-C₁₋₃alkyl chain to form a 5-7 membered ring;
- 10 R¹⁷ is selected from: hydrogen, C₁₋₆alkyl, unsubstituted or substituted with 1-6 substituents selected from: fluoro, C₁₋₃alkoxy, hydroxyl and -COR¹¹, COR¹¹, hydroxy, and -O-C₁₋₆alkyl, unsubstituted or substituted with 1-6 substituents selected form: fluoro, C₁₋₃alkoxy, hydroxy, and -COR¹¹, or
- R^{16} and R^{17} may be joined together by a C_{1-4} alkyl chain or a C_{0-3} alkyl-O- C_{0-3} alkyl chain to form a 3-6 membered ring;

- R^{18} is selected from: hydrogen, C_{1-6} alkyl, unsubstituted or substituted with 1-6 fluoro, fluoro, $O-C_{3-6}$ cycloalkyl, and - $O-C_{1-3}$ alkyl, unsubstituted or substituted with 1-6 fluoro, or
- R^{16} and R^{18} are joined together by a $C_{2\text{-3}}$ alkyl chain to form a 5-6 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, - COR^{11} , $C_{1\text{-3}}$ alkyl, and $C_{1\text{-3}}$ alkoxy, or
- R¹⁶ and R¹⁸ are joined together by a C₁₋₂alkyl-O-C₁₋₂alkyl chain to form a 6-8 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -COR¹¹, C₁₋₃alkyl, and C₁₋₃alkoxy, or

 R^{16} and R^{18} are joined together by a -O-C₁₋₂alkyl-O-chain to form a 6-7 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -COR¹¹, C₁₋₃alkyl, and C₁₋₃alkoxy;

R¹⁹ is selected from: hydrogen, phenyl, C₁₋₆alkyl substituted or unsubstituted with 1-6 substituents selected from: -COR¹¹, hydroxy, fluoro, chloro and -O-C₁₋₃alkyl;

 R^{24} and R^{25} are independently selected from: =O, where one of R^{24} and R^{25} is oxygen bound via a double bond. hydrogen, phenyl, and C_{1-6} alkyl, substituted or unsubstituted with 1-6 substituents selected from: -COR¹¹, hydroxy, fluoro, chloro, -O-C₁₋₃alkyl;

m is 0, 1 or 2;

n is 1 or 2;

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the dashed line represents a single or a double bond; and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

2. The compound of claim 1 of the formula Ia:

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Ιa

and pharmaceutically acceptable salts and individual diastereomers thereof.

3. The compound of claim 1 of the formula IIa:

$$R^7$$
 R^9
 N
 $1-2$
 N
 R^5
 R^3

Πa

and pharmaceutically acceptable salts and individual diastereomers thereof.

4. The compound of claim 1 of the formula Ib:

Ιb

- and pharmaceutically acceptable salts and individual diastereomers thereof.
 - 5. The compound of claim 1 of the formula IIb:

15 IIb

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and pharmaceutically acceptable salts and individual diastereomers thereof.

6. The compound of claim 1 of the formula Ic:

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Ic

and pharmaceutically acceptable salts and individual diastereomers thereof.

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- 7. The compound of claim 1, wherein X is C, O or N.
- 8. The compound of claim 1, wherein X is C.

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- 9. The compound of claim 1, wherein Y is -CH₂- or -O-
- 10. The compound of claim 1, wherein R¹ is selected from: -C₁₋₆alkyl, -C₀₋₆alkyl-O-C₁₋₆alkyl, heterocycle, and -(C₀₋₆alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl), where the alkyl, heterocycle, and the cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C₁₋₃alkyl, trifluoromethyl, C₁₋₃alkyl, -O-C₁₋₃alkyl, -COR¹¹, -CN, -NR¹²R¹², and -CONR¹²R¹².
- 11. The compound of claim 1, wherein R¹ is selected from: -C₁-6alkyl, unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, -O-C₁-3alkyl, trifluoromethyl, and -COR¹¹; -C₀-6alkyl-O-C₁-6alkyl-, unsubstituted or substituted with 1-6 substituents independently selected from: halo, trifluoromethyl, and -COR¹¹; and -(C₃-5cycloalkyl)-(C₀-6alkyl), unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C₁-3alkyl, trifluoromethyl, and -COR¹¹.
- 25 12. The compound of claim 1, wherein R¹ is selected from: C₁₋₆alkyl, C₁₋₆alkyl substituted with hydroxyl, and C₁₋₆alkyl substituted with 1-6 fluoro.

The compound of claim 1, wherein R¹ is selected from: -CH(CH₃)₂, -13. CH(OH)CH₃, -C(OH)(CH₃)₂, and -CH₂CF₃.

- The compound of claim 1, wherein R² is hydrogen. 14.
 - 15. The compound of claim 1, wherein R³ is nothing.
 - The compound of claim 1, wherein R⁴ is hydrogen. 16.

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- The compound of claim 1, wherein R⁵ is selected from: C₁₋₆alkyl 17. substituted with 1-6 fluoro, -O-C1-6alkyl substituted with 1-6 fluoro, chloro, bromo, and phenyl.
- The compound of claim 1, wherein which R⁵ is selected from: 18. trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl. 15
 - The compound of claim 1, wherein R⁵ is trifluoromethyl. 19.
 - The compound of claim 1, wherein R⁶ is hydrogen. 20.

- The compound of claim 1, wherein R⁷ is selected from phenyl. 21. heterocycle, C₃₋₇cycloalkyl, C₁₋₆alkyl, -COR¹¹, and -CONH-V-COR¹¹, where V is selected from C₁₋₆alkyl and phenyl, and where the phenyl, heterocycle, C₃₋₇cycloalkyl, and C₁₋₆alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C1-3alkyl, -O-C1-3alkyl, -COR11, -CN, -heterocycle, and -
- 25 CONR12R12.
 - The compound of claim 1, wherein, when X is not O, R⁷ is selected from 22. phenyl, heterocycle, C₁₋₄alkyl, -COR¹¹ and -CONH-V-COR¹¹, where V is selected from C₁₋

₆alkyl or phenyl, where the phenyl, heterocycle, and C_{1-4} alkyl is unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C_{1-3} alkyl, -O- C_{1-3} alkyl, -COR¹¹, and -heterocycle.

- 5 23. The compound of claim 1, wherein X is O, and R⁷ and R⁸ are nothing.
 - 24. The compound of claim 1, wherein X is C, and R⁸ is hydrogen.
- 25. The compound of claim 1, wherein which R⁹ is selected from: hydrogen, 10 hydroxy, -CH₃, -O-CH₃, and =O, where R⁹ is joined to the ring via a double bond.
 - 26. The compound of claim 1, wherein R⁹ is hydrogen.
 - 27. The compound of claim 1, wherein R¹⁰ is hydrogen.

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- 28. The compound of claim 1, wherein R¹⁵ is hydrogen or methyl.
- 29. The compound of claim 1, wherein R¹⁶ is selected from: hydrogen, C₁₋₃alkyl, unsubstituted or substituted with 1-6 fluoro, -O-C₁₋₃alkyl, fluoro, and hydroxy.
- 30. The compound of claim 1, wherein R¹⁶ is selected from: hydrogen, trifluoromethyl, methyl, methoxy, ethoxy, ethyl, fluoro, and hydroxy.
 - 31. The compound of claim 1, wherein \mathbb{R}^{17} is hydrogen.
- 32. The compound of claim 1, wherein R^{18} is selected from: hydrogen, methyl, and methoxy.
 - 33. The compound of claim 1, wherein R¹⁸ is hydrogen.

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34. The compound of claim 1, wherein R¹⁶ and R¹⁸ are joined together by a - CH₂CH₂- chain or a -CH₂CH₂- chain to form a cyclopentyl ring or a cyclohexyl ring.

- 5 35. The compound of claim 1, wherein R¹⁹ is hydrogen.
 - 36. The compound of claim 1, wherein R²⁴ is hydrogen.
 - 37. The compound of claim 1, wherein R^{25} is =0.
 - 38. The compound of claim 1, wherein m = 0 or 1.
 - 39. The compound of claim 1, wherein n = 1 or 2.
- 15 40. A compound selected from:

- 41. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.
- 5 42. A method for modulation of chemokine receptor activity in a mammal which comprises the administration of an effective amount of a compound of Claim 1.

43. A method for treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease which comprises the administration to a patient of an effective amount of a compound of Claim 1.

5 44. A method for treating, ameliorating, controlling or reducing the risk of rheumatoid arthritis which comprises the administration to a patient of an effective amount of a compound of Claim 1.